

# PATENT COOPERATION TREATY

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From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

2.1 JUL 2005 **PCT**

To:

GLOBAL INTELLECTUAL PROPERTY  
AstraZeneca AB  
SE-151 85 Södertälje  
SUEDE

ASTRA ZENECA PLC  
GLOBAL INTELLECTUAL

CODE	DATE	NTD

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(PCT Rule 71.1)

ANKOM 1 8 JUL 2005

GIPS

Date of mailing  
(day/month/year)

15.07.2005

DATA

Applicant's or agent's file reference  
101064-1 WO

ENTERED  
FINAL  
CHECK

**IMPORTANT NOTIFICATION**

International application No.  
PCT/GB2004/003473

International filing date (day/month/year)  
12.08.2004

Priority date (day/month/year)  
15.08.2003

Applicant  
ASTRAZENECA AB

- The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.
- A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
- Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international  
preliminary examining authority:



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**PATENT COOPERATION TREATY**  
**PCT**  
**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**  
(Chapter II of the Patent Cooperation Treaty)  
(PCT Article 36 and Rule 70)

CODE	DATE	NTD
ANKOM 18 JUL 2005		GIPS
DATA ENTERED		
FINAL CHECK		

Applicant's or agent's file reference 101064-1 WO		<b>FOR FURTHER ACTION</b> See Form PCT/PEA416	
International application No. PCT/GB2004/003473	International filing date (day/month/year) 12.08.2004	Priority date (day/month/year) 15.08.2003	
International Patent Classification (IPC) or national classification and IPC C07D333/38, C07D409/12, A61K31/38, A61P35/00			
Applicant ASTRAZENECA AB			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand  02.06.2005		Date of completion of this report  15.07.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80288 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer  Bakboord, J Telephone No. +49 89 2399- 	

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**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/GB2004/003473

1AP20 REC'D PCT/PTO 14 FEB 2006

**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
    - ☐ international search (under Rules 12.3 and 23.1(b))
    - ☐ publication of the international application (under Rule 12.4)
    - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

**Description, Pages**

1-79 as originally filed

**Claims, Numbers**

1-28 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
    - ☐ the description, pages
    - ☐ the claims, Nos.
    - ☐ the drawings, sheets/figs
    - ☐ the sequence listing (*specify*):
    - ☐ any table(s) related to sequence listing (*specify*):
  4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
    - ☐ the description, pages
    - ☐ the claims, Nos.
    - ☐ the drawings, sheets/figs
    - ☐ the sequence listing (*specify*):
    - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/GB2004/003473

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 20-25

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 20-25

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/GB2004/003473

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	2-5, 7, 9, 11-17
	No: Claims	1, 6, 8, 10, 18-27, 28
Inventive step (IS)	Yes: Claims	1-17
	No: Claims	1-28
Industrial applicability (IA)	Yes: Claims	1-19, 26-28
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(SEPARATE SHEET)**

International application No.

PCT/GB2004/003473

**III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 20-25 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

V.1 The present application relates to 2-ureido-3-amido-5-phenyl substituted thiophenes and their use as checkpoint kinase 1 inhibitors.

V.2 Reference is made to the following documents:

D1: WO 03/029241 A

D2: WO 03/028731 A

D3: WO 02/070494 A

**V.3 Novelty**

Document D1 discloses a compound of formula I in which R<sup>1</sup> is hydrogen, R<sup>2</sup> is methyl, R<sup>4</sup> is methyl and R<sup>5</sup> is methyl (example 28). Moreover document D1 discloses 2-ureido-3-amido-5-phenyl substituted thiophenes and their use as checkpoint kinase 1 inhibitors (claim 5).

Document D1 also discloses the use of a compound of formula VI in the manufacture of a compound of formula I (scheme II).

Document D2 discloses 2-amido-3-ureido-5-phenyl substituted thiophenes and their use as checkpoint kinase 1 inhibitors (claim 6).

Document D3 discloses phenyl rings substituted with groups C(O)NR<sup>1</sup>R<sup>2</sup>, N(H)C(O)N(H)R<sup>4</sup> and OR<sup>5</sup> (see e.g. compounds 1-6) to be used as checkpoint kinase 1 inhibitors.

A compound of formula I for the use as checkpoint inhibitors is disclosed in document D1. Claims 1, 6, 8, 10, 18-27 therefore do not fulfill the requirements of

Article 33(2) PCT.

A compound of formula I as described in claims 2-5, 7, 9, 11-17 is disclosed in none of the documents. These claims therefore fulfill the requirements of Art 33(2) PCT.

The use of a compound of formula VI for the manufacture of a compound of formula I is disclosed in document D1. Claim 28 therefore does not fulfill the requirements of Art 33(2) PCT.

**V.4 Inventive step**

As the use of thiophene 2-ureido-3-amido-5-phenyl substituted thiophenes for the inhibition of checkpoint kinase 1 is known from document D1 the present application cannot be considered to involve an inventive step (Art 33(3) PCT).

**V.5 Industrial applicability**

For the assessment of the present claims 20-25 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.